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MEMORANDUM

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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

SUBJECT: **Cocamide DEA** Quantitative Risk Assessment (Q_1^*) Based On B6C3F1 Mouse Dietary Study Using mg/kg b.w.$^{3/4}$'s/day Cross Species Scaling Factor

P.C. Code 224600

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The most potent unit risk, Q_1^*(mg/kg/day)$^{-1}$, of those calculated for Cocamide DEA and DEA, a contaminant of commercial diethanolamide preparations, is that for DEA at 4.01×10^{-1} in human equivalents based on male mouse liver adenoma, carcinoma and/or hepatoblastoma combined tumor rates. The dose levels used from the 104-week dermal study were 0, 40, 80, and 160 mg/kg/day of DEA. The corresponding tumor rates were 39/50, 47/50, 50/50, and 49/50, respectively.

Background

On July 25, 2001, the Cancer Assessment Review Committee met to classify the carcinogenic potential of Cocamide DEA Quantifications of risk have subsequently been estimated for male and female mouse liver and kidney tumors for both Cocamide DEA and DEA, a contaminant of commercial diethanolamide preparations. The most potent unit risk will be used for the purpose of lifetime cancer risk assessment by the Agency. In this case, the most potent unit risk, Q_1^*, is that for DEA male mouse liver adenoma, carcinoma and/or hepatoblasoma combined tumor rates at 4.01×10^{-1} in human equivalents.

All unit risks have been converted from animals to humans by use of the $^3/_4$'s scaling factor (Tox_Risk program, Version 3.5, K. Crump, 1994)[1]. For the conversion to human equivalents, weights of 0.03 kg for the mouse and 70 kg for humans were used.

It is to be noted that the Q_1^* $(mg/kg/day)^{-1}$ is an estimate of the upper bound on risk and that, as stated in the EPA Risk Assessment Guidelines, the true value of the risk is unknown, and may be as low as zero.

Dose-Response Analysis

The statistical evaluation of mortality by NTP showed no statistically significant increases in mortality with increasing doses of Cocamide DEA or DEA in male or female mice. The unit risk, Q_1^*, was obtained by the application of the Multi-Stage model (Tox_Risk program, Version 3.5, K. Crump, 1994).

Cocamide DEA Study

Male mice had a significant increasing trend at $p < 0.01$, and a significant difference in the pair-wise comparison of the 200 mg/kg/day dose group with the controls at $p < 0.05$, for kidney adenomas. There was a significant increasing trend, and a significant difference in the pair-wise comparison of the 200 mg/kg/day dose group with the controls, for kidney adenomas and/or carcinomas combined, both at $p < 0.01$. There was a significant increasing trend, and significant differences in the pair-wise comparisons of the 100 and 200 mg/kg/day dose groups with the controls, for liver adenomas, all at $p < 0.01$. There was a significant increasing trend at $p < 0.01$, and significant differences in the pair-wise comparisons of the 100 ($p < 0.05$) and 200 ($p < 0.01$) mg/kg/day dose groups with the controls, for liver adenomas and/or carcinomas combined. There were also significant increasing trends, and significant differences in the pair-wise comparisons of the 200 mg/kg/day dose group with the controls, for liver hepatoblastomas, and adenomas, carcinomas and/or hepatoblatomas combined, all at $p < 0.01$. There was a significant difference in the pair-wise comparison of the 100 mg/kg/day dose group with the controls for liver adenomas, carcinomas and/or hepatoblatomas combined at $p < 0.05$.

Female mice had significant increasing trends, and significant differences in the pair-wise comparisons of the 100 and 200 mg/kg/day dose groups with the controls, for liver adenomas, carcinomas, adenomas and/or carcinomas combined, and adenomas, carcinomas and/or hepatoblastomas combined, all at $p < 0.01$.

DEA Study

Male mice had significant increasing trends, and significant differences in the pair-wise comparisons of the 80 and 160 mg/kg/day dose groups with the controls, for liver adenomas, carcinomas, and adenomas, carcinomas and/or hepatoblastomas combined, all at $p < 0.01$. There were significant differences in the pair-wise comparisons of the 40 mg/kg/day dose group with the controls for liver adenomas, and adenomas, carcinomas and/or hepatoblastomas combined, both at $p < 0.05$. There was a significant increasing trend at $p < 0.01$, and significant differences in the pair-wise comparisons of the 80 ($p < 0.01$) and 160 ($p < 0.05$) mg/kg/day dose groups with the controls, for liver hepatoblastomas.

Female mice had significant increasing trends, and significant differences in the pair-wise comparisons of the 80 and 160 mg/kg/day dose groups with the controls, for liver adenomas, carcinomas, and adenomas, carcinomas and/or hepatoblastomas combined, all at $p < 0.01$. There were significant differences in the pair-wise comparisons of the 40 mg/kg/day dose group with the controls for liver adenomas, and adenomas, carcinomas and/or hepatoblastomas combined, both at $p < 0.05$. There was also a significant difference in the pair-wise comparison of the 40 mg/kg/day dose group with the controls for liver carcinomas at $p < 0.01$.

<u>Additional Q_1^* Calculations</u>

The unit risk, $Q_1^*(mg/kg/day)^{-1}$, of Cocamide DEA based upon male mouse kidney adenoma and/or carcinoma combined tumor rates is 7.50×10^{-3} in human equivalents. The dose levels used from the 104-week dermal study were 0, 100, and 200 mg/kg/day of Cocamide DEA. The corresponding tumor rates were 1/50, 1/50, and 9/50, respectively.

The unit risk, $Q_1^*(mg/kg/day)^{-1}$, of Cocamide DEA based upon male mouse liver adenoma and/or carcinoma combined tumor rates is 1.17×10^{-1} in human equivalents. The dose levels used from the 104-week dermal study were 0, 100, and 200 mg/kg/day of Cocamide DEA. The corresponding tumor rates were 28/50, 39/50, and 47/50, respectively.

The unit risk, $Q_1^*(mg/kg/day)^{-1}$, of Cocamide DEA based upon male mouse liver adenoma, carcinoma and hepatoblastoma combined tumor rates is 1.02×10^{-1} in human equivalents. The dose levels used from the 104-week dermal study were 0, 100, and 200 mg/kg/day of Cocamide DEA. The corresponding tumor rates were 29/50, 39/50, and 49/50, respectively.

The unit risk, $Q_1^*(mg/kg/day)^{-1}$, of Cocamide DEA based upon female mouse liver adenoma, carcinoma and/or hepatoblastoma combined tumor rates is 1.76×10^{-1} in human equivalents. The dose levels used from the 104-week dermal study were 0, 100, and 200 mg/kg/day of Cocamide DEA. The corresponding tumor rates were 33/50, 46/50, and 48/50, respectively.

The unit risk, $Q_1^*(mg/kg/day)^{-1}$, of DEA based upon female mouse liver adenoma, carcinoma and hepatoblastoma combined tumor rates could not be fit to the model due to the fact that all of the dosed groups achieved 100% tumor rates. The dose levels used from the 104-week dermal study were 0, 40, 80, and 160 mg/kg/day of DEA. The corresponding tumor rates were 33/50, 50/50, 50/50, and 50/50, respectively.

The above calculations were generated at the recommendation of the CARC committee. Further calculations by the Agency should be based on the most potent unit risk, $Q_1^*(mg/kg/day)^{-1}$, of those calculated for Cocamide DEA and DEA, a contaminant of commercial diethanolamide preparations, which is that for DEA at 4.01×10^{-1} in human equivalents based on male mouse liver adenoma, carcinoma and/or hepatoblastoma combined tumor rates. The dose levels used from the 104-week dermal study were 0, 40, 80, and 160 mg/kg/day of DEA. The corresponding tumor rates were 39/50, 47/50, 50/50, and 49/50, respectively.

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